

oligonucleotide comprises at least one heteroatomic backbone modification and a 2'-alkoxyalkoxy modification.

**REMARKS**

Claims 1, 8, 10-18, 27-29, and 31-33 are pending in this patent application.

The Office Action indicates that the PTO has misplaced certain references identified in Applicants' information disclosure statement. In this respect, the Examiner's attention is directed to the enclosed copy of a return postcard indicating receipt of all cited references by the PTO mailroom on April 24, 2000. Applicants request clarification as to the nature of the search for such misplaced references. Assuming that the PTO has searched for the references and that they are still missing, Applicants are willing to cooperate with the PTO to locate replacement copies thereof. Otherwise, Applicants request that each reference cited in the present information disclosure statement formally be made of record. Enclosed herewith are replacement copies of Applicants' Forms PTO-1449 to facilitate that process.

Claims 1, 8, and 10-16 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 of U.S. Patent No. 5,789,573 ("the 573 Patent"), taken alone or in combination with certain references. Applicants do not necessarily agree that those skilled in the art would have found the subject matter of their claims to have been obvious in view of the claims of the 573 Patent. Nonetheless, the rejection likely can be resolved upon the Examiner's identification of allowable subject matter through the filing of a suitable terminal disclaimer.

The Office Action requests confirmation that the inventions recited in claims 1, 8, and 10 and those claimed in the 573 Patent were, at the time the inventions were made, owned by the same person or subject to an obligation of assignment to the same person. Applicants' Assignee hereby provides such confirmation pursuant to 37 C.F.R. 1.78(c).<sup>1</sup>

Claims 17 and 18 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1 and 5-7 of U.S. Patent No. 6,087,489 ("the 489 Patent"). Applicants do not necessarily agree that those skilled in the art would have found the subject matter of their claims to have been obvious in view of the claims of the 489 Patent. Nonetheless, the rejection likely can be resolved upon the Examiner's identification of allowable subject matter through the filing of a suitable terminal disclaimer.

The Office Action requests confirmation that the subject matter and the inventions recited in claims 17 and 18 and those claimed in the 489 Patent were, at the time the inventions were made, owned by the same person or subject to an obligation of assignment to the same person. Applicants' Assignee hereby provides such confirmation pursuant to 37 C.F.R. 1.78(c).

Claims 27-31 and 33 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over certain claims of Application Serial No. 08/847,151. Applicants request that this rejection be deferred pending some identification of allowable subject matter, as it likely can be readily resolved (depending upon the subject matter ultimately allowed) through the filing of a suitable terminal disclaimer.

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<sup>1</sup> It is unclear why the Office Action at pages 5 and 9 refers to 35 U.S.C. § 132, which does not appear to relate to the issue of common ownership.

Claims 27-30 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicants respectfully request reconsideration of this rejection, as there is no reason of record to believe that those skilled in the art would not be able to practice the claimed inventions to at least some measurable extent.

Although the Office Action cites a number of references for the proposition that certain compounds recited in the claims might undergo a degree of depurination, there is no reason of record to believe that depurination will occur to such an extent that persons skilled in the art will not be able to practice the claimed methods and obtain a measurable result. The Office Action identifies certain problems that allegedly would be encountered in practicing the claimed methods -- and criticizes Applicants' specification for allegedly not addressing these problems -- but there is no requirement in the patent laws that patentable inventions be problem-free, or that a patent specification address all potential problems that might be encountered in practicing an invention. In fact, it is improper for the PTO to require any showing regarding the degree of effectiveness of therapeutic inventions, such as those now claimed M.P.E.P. § 2107.02; *In re Sichert*, 566 F.2d 1154 (C.C.P.A. 1977).

Not only does the mere existence of problems associated with the claimed inventions not negate their patentability, but such problems are actually to be *expected*. It is well-established that pharmaceutical inventions usually require further research and development. *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). Were such inventions not patentable long before being optimized or ready for human use, the incentive to research and develop vital drugs and potential cures would be completely removed. *Id.* at 1567-68.

Although the Office Action relies upon a number of references for their alleged disclosure of "problems," the references nowhere so much as suggests that these "problems" are so significant as to prevent the claimed methods from producing measurable results. In fact, the cited Rojanasakul reference specifically states that "there are numerous studies demonstrating the effectiveness of antisense ONs in various cells culture systems," and that "several ON drugs have already demonstrated enough promise to justify clinical trials" (Rojanasakul reference at page 118 and 126, respectively). Thus, to the extent that "problems" are identified, such "problems" relate to optimizing the performance of a therapeutic product, and not to simply obtaining measurable results. Since there is no requirement that an invention be optimized to be patentable, the references cited in the Office Action fail to support rejection of Applicants' claims.

Claims 1, 8, and 10 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by the 573 Patent. The Office Action, however, does not identify any portion of the 573 Patent that discloses a compound having all of the features recited in Applicants' claims. Although the Office Action notes that isolated dependent claims in the 573 Patent recite certain of the features of Applicants' claims, and that the independent claim of the 573 Patent is broad enough to include certain of Applicants' claimed compounds, much more is required to establish anticipation. As will be recognized, an anticipatory reference must "clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference." *In re Arkley*, 455 F.2d 586, 587 (C.C.P.A. 1972). Since the outstanding rejection is

predicated upon such improper "picking, choosing and combining," Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claims 17 and 18 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by the 489 Patent. The 489 Patent, however, does not constitute prior art under § 102(e), as the patent application from which it issued was filed on June 2, 1998, after Applicants' April 30, 1997, effective filing date for the claimed subject matter. Accordingly, the rejection for alleged anticipation in view of the 489 Patent should be withdrawn.

Claims 1, 8, and 10-18 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable in view of the combined teaching of Hanacek, *et al.*, *J. Virol.* **1996**, 70, 5203 ("the Hanacek reference"), Milligan, *et al.*, *J. Med. Chem.* **1993**, 36, 1923 ("the Milligan reference"), U.S. Patent No. 5,739,118 ("the Carrano patent"), and U.S. Patent No. 5,795,870 ("the Kahne patent"). Applicants respectfully request reconsideration of this rejection, as combination of the cited references in accordance with their respective teachings would not have produced any claimed invention.

As best understood, what the Office Action alleges is that it would have been obvious to those of ordinary skill in the art to take one of the 2'-alkoxyalkyl-substituted oligonucleotides disclosed by the Hanacek reference and to then modify it in accordance with the teaching of, *inter alia*, the Carrano patent. As will be recognized, what the Carrano patent teaches is placement of an "antisense molecule" of interest in an expression vector or some other "genetic material which acts as a template for copies" thereof (*see, e.g.*, column 11, lines 58-60 and Figures 1-4). Thus, the product produced by a person of ordinary skill who did not have the benefit of Applicants disclosure

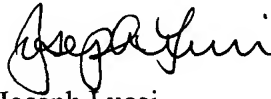
but was nonetheless attempting to combine the teaching Hanacek reference with the teaching of the Carrano patent and the other applied references would have been an expression vector containing the Hanacek oligonucleotide.

This product would have been different from any of Applicants' claimed inventions. Indeed, none of Applicants claims 1, 8, and 10-18 are directed to the expression vectors that the combination would have produced. Rather, they are directed to oligonucleotides and pharmaceutical compositions that contain oligonucleotides.

Since those of ordinary skill would not have produced any claimed invention, even if it were assumed for the sake of argument that they would have been motivated to combine the respective teachings of the cited references (and Applicants do not believe that they would have been motivated to make the combination), Applicants respectfully request that the rejection for alleged obviousness be reconsidered and withdrawn. *In re Payne*, 203 U.S.P.Q. 245, 255 (C.C.P.A. 1979) (references relied upon to support rejection under § 103 must place the claimed invention in the possession of the public).

In view of the foregoing, Applicants submit that the claims presently before the Examiner are in condition for allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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